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1 GAATTCCCAA AGACAAAtg gattttcaag tgcagatttt cagcttcctg
51 ctaatacagtg cctcagtcac aatatccaga ggacaaattg ttctcaccac
101 gtctccagca atcatgtctg catctccagg ggagaagggtc accatgacct
151 gcagtgccag ctcaagtgtg agttacatga actggtacca gcagaagtca
201 ggcacctccc ccaaaagatg gatttatgac acatccaaac tggcttctgg
251 agtccctgct cacttcaggg gcagtgggtc tgggacctct tactctctca
301 caatcagcgg catggaggct gaagatgctg ccacttatta ctgccagcag
351 tggagtagta accattcac gttcgggtcg gggacaaagt tggaaataaa
401 ccgggctgat actgcaccaa ctgtatccat cttcccacca tccagtgagc
451 agttaacatc tggagggtgc tcagtcgtgt gcttcttgaa caacttctac
501 cccaaagaca tcaatgtcaa gtggaagatt gatggcagtg aacgacaaaa
551 tggcgtcctg aacagttgga ctgatcagga cagcaaagac agcacctaca
601 gcatgagcag caccctcacg ttgaccaagg acgagtatga acgacataac
651 agctataacct gtgaggccac tcacaagaca tcaacttcac ccattgtcaa
701 gagcttcaac aggaatgagt gtTAGAGACA AAGGTCCTGA GACGCCACCA
751 CCAGCTCCCA GCTCCATCCT ATCTTCCCTT CTAAGGTCTT GGAGGCTTCC
801 CCACAAGCGC tTACCACTGT TGGGCTGCTC TAAACCTCCT CCCACCTCCT
851 TCTCCTCCTC CTCCCTTTCC TTGGCTTTTA TCATGCTAAT ATTTGCAGAA
901 AATATTCAAT AAAGTGAGTC TTTGCCTTGA AAAAAAAAAA AAA
(SEQ ID NO: 4)

FIG. 1a

1 MDFQVQIFSF LLISASVIIS RGDQIVLTQSP AIMSASPGEK VTMTCSASSS
51 VSYMNWYQQK SGTSPKRWIY DTSKLASGVP AHFRGSGSGT SYSLTISGME
101 AEDAATYYCQ QWSSNPFTFG SGTKLEINRA DTAPTVSIFP PSSEQLTSGG
151 ASVVCFLNNF YPKDINVKWK IDGSRQNGV LNSWTDQDSK DSTYSMSSTL
201 TLTKEDEYERH NSYTCEATHK TSTSPIVKSF NRNEC* (SEQ ID NO: 5)

FIG. 1b

Application No.: 08/846,658

Title: Humanised Antibodies

Inventors: John R. Adair, Diljeet S. Athwal and John S. Emtage

Docket No. CARP-0057

Atty: Doreen Yatko Trujillo

Date of Filing: May 1, 1997

Telephone No. (215) 568-3100

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1  GAATTCCCCT CTCCACAGAC ACTGAAAAC CTGACTCAAC ATGGAAAGGC
51  ACTGGATCTT TCTACTCCTG TTGTCAGTAA CTGCAGGTGT CCACTCCCAG
101 GTCCAGCTGC AGCAGTCTGG GGCTGAACTG GCAAGACCTG GGGCCTCAGT
151 GAAGATGTCC TGCAAGGCTT CTGGCTACAC CTTTACTAGG TACACGATGC
201 ACTGGGTAAA ACAGAGGCCT GGACAGGGTC TGGAAATGGAT TGGATACATT
251 ATTCCTAGCC GTGGTTATAC TAATTACAAT CAGAAGTTCA AGGACAAGGC
301 CACATTGACT ACAGACAAAT CCTCCAGCAC AGCCTACATG CAACTGAGCA
351 GCCTGACATC TGAGGACTCT GCAGTCTATT ACTGTGCAAG ATATTATGAT
401 GATCATTACT GCCTTGACTA CTGGGGCCAA GGCACCACTC TCACAGTCTC
451 CTCAGCCAAA ACAACAGCCC CATCGGTCTA TCCACTGGCC CCTGTGTGTG
501 GAGATACAAC TGGCTCCTCG GTGACTCTAG GATGCCTGGT CAAGGGTTAT
551 TTCCCTGAGC CAGTGACCTT GACCTGGAAC TCTGGATCCC TGTCCAGTGG
601 TGTGCACACC TTCCCAGCTG TCCTGCAGTC TGACCTCTAC ACCCTCAGCA
651 GCTCAGTGAC TGTAACCTCG AGCACCTGGC CCAGCCAGTC CATCACCTGC
701 AATGTGGCCC ACCCGGCAAG CAGCACCAAG GTGGACAAGA AAATTGAGCC
801 ACCTCTTGGG TGGACCATCC GTCTTCATCT TCCCTCCAAA GATCAAGGAT
851 GTACTIONGA TCTCCCTGAG CCCCATAGTC ACATGTGTGG TGGTGGATGT
901 GAGCGAGGAT GACCCAGATG TCCAGATCAG CTGGTTTGTG AACACGTGG
951 AAGTACACAC AGCTCAGACA CAAACCCATA GAGAGGATTA CAACAGTACT
1001 CTCCGGGTGG TCAGTGCCCT CCCCATCCAG CACCAGGACT GGATGAGTGG
1051 CAAGGAGTTC AAATGCAAGG TCAACAACAA AGACCTCCCA GCGCCCATCG
1101 AGAGAACCAT CTCAAAACCC AAAGGGTCAG TAAGAGCTCC ACAGGTATAT
1151 GTCTTGCCCTC CACCAGAAGA AGAGATGACT AAGAAACAGG TCACTCTGAC
1201 CTGCATGGTC ACAGACTTCA TGCCTGAAGA CATTTACGTG GAGTGGACCA
1251 ACAACGGGAA AACAGAGCTA AACTACAAGA AACTGAACC AGTCCTGGAC
1301 TCTGATGGTT CTTACTTCAT GTACAGCAAG CTGAGAGTGG AAAAGAAGAA
1351 CTGGGTGGAA AGAAATAGCT ACTCCTGTTT AGTGGTCCAC GAGGGTCTGC
1401 ACAATACCA CACGACTAAG AGCTTCTCCC GGACTIONGGG TAAATGAGCT
1451 CAGCACCCAC AAAACTCTCA GGTCCAAAGA GAGACCCACA CTCATCTCCA
1501 TGCTTCCCTT GTATAAATAA AGCACCCAGC AATGCCTGGG ACCATGTAAA
1551 AAAAAAAAAA AAAGGAATTC (SEQ ID NO:6)

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FIG. 2a

OKT 3 HEAVY CHAIN PROTEIN SEQUENCE DEDUCED FROM DNA SEQUENCE

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1  MERHWIFLLL LSVTAGVHSQ VQLQQSGAEL ARPGASVKMS CKASGYTFTR
51 YTMHWVKQRP GQGLEWIGYI NPSRGYTNYN QKFKDKATLT TDKSSSTAYM
101 QLSSLTSEDS AVYYCARYYD DHYCLDYWGQ GTTLTVSSAK TTAPSVYPLA
151 PVCGDTTGSS VTLGCLVKGY FPEPVTLTWN SGSLSSGVHT FPAVLQSDLY
201 TLSSSVTVTS STWPSQSITC NVAHPASSTK VDKKIEPRGP TIKPCPPCKC
251 PAPNLLGGPS VFIFPPKIKD VLMISLSPIV TCVVVDVSED DPDVQISWV
301 NNVEVHTAQT QTHREDYNST LRVVSALPIQ HQDWMSGKEF KCKVNNKDLP
351 APIERTISKP KGSVRAPQVY VLPPPEEEMT KKQVTLTCMV TDFMPEDIYV
401 EWTNNGKTEL NYKNTEPVLD SDGSYFMYSK LRVEKKNWVE RNSYSCSVVH
451 EGLHNHHTTK SFSRTPGK* (SEQ ID NO: 7)
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FIG. 2b

Application No.: 08/846,658

Title: Humanised Antibodies

Inventors: John R. Adair, Diljeet S. Athwal and John S. Emtage

Docket No. CARP-0057

Date of Filing: May 1, 1997

Atty: Doreen Yatko Trujillo

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```

1                23                42
NN              N                N    N    N
RES TYPE      SBSpSPESsSBSbSsSsSPSPSPsPSsse*s*p*Pi^ISsSe
Dkt3vl       QIVLTQSPA1MSASPGEKVTMTCSASS.SVSYMNWYQQKSGT
REI          DIQMTQSPSSLSASVGDRVTITCQASQDI23IKYLNWYQQI42PGK
? ?
      CDR1    (LOOP)          *****
      CDR1    (KABAT)        *****

                    56                85
N  NN
RES TYPE      *IsiPpIeesesssSBEsePsPSBSSEsPspSPsseesSPePb
Dkt3vl       SPKRWIYDTSKLASGVPAHF56RGSGSGTSYSLTISGMEAE85DAAT
REI          APKLLIYEASN56LQAGVPSRFSGSGSGTDYTETISSLQPEDIAT (SEQ
ID NO:8)      ? ??                ? ?
                ***** CDR2 (LOOP/KABAT)

                    102    108
RES TYPE      PiPIPIes**iPIIsPPSPSPSS
Dkt3vl       YYCQQWSSNPFTFGSGTKLEINR (SEQ ID NO:29)
REIvl       YYCQQYQSLPYTFGQGT102KLQI108IR (SEQ ID NO:9)
                ?      ?
                ***** CDR3 (LOOP)
                ***** CRD3(KABAT)

```

FIG. 3

Application No.: 08/846,658

Title: Humanised Antibodies

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```

NN N                23 26    32 35  N39  43
RES TYPE  SESPs^SBssSsSSssSpSpSPsPSEbSBssBePi^PIpiesss
Dkt3h     QVQLQQSGAELARPGASVKMSCKASGYTFTRYTMNHWVKQRPGQ
KOL       QVQLVESGGGVVQPGRSLRLSCSSSGFIFSSYAMYWVRQAPGK
           ?                ??

                               ***** CDR1 (LOOP)
                               ***** CDR1 (KABAT)

52a    60    65    N N N    82abc    89
RES TYPE IIEIppp^ssssssss^ps^pSSsbSpseSsSseSp^pSpSssS^ePb
Dkt3vh   GLEWIGYINPSRGYTNTNQKFKRKATLTTDKSSSTAYMQLSSLTSEDSAV
KOL      GLEWVAIIWDDGSDQHYADSVKGRFTISRDNSKNTLELQMDSLPPEDTGV
           ??                ? ? ? ? ?

                               ***** CDR2 (LOOP)
                               ***** CDR2 (KABAT)

92 N                107    113
RES TYPE  PiPIEissssiisssbibi*EIPIP*spSBSS
Dkt3vh    YYCARYYDDHY.....CLDYWGQGTTLTVSS (SEQ ID NO:30)
KOL       YFCARDGGHGFCSSASCFGPDYWGQGTPTVTVSS (SEQ ID NO:10)
           ***** CRD4 (KABAT/LOOP)

```

FIG. 4

Application No.: 08/846,658

Title: Humanised Antibodies

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DKT 3 HEAVY CHAIN CDR GRAFTS

1. gh341 and derivatives

	1	26	35	39	43	
Dkt3vh	QVQLQQSGAELARPGASVKMSCKASGYTFTRYTMHWVKQRPGQ					
gh341	QVQLVESGGGVVQDGRSLRLSCSSSGYTFTRYTMHWVRQAPGK					JA178
gh341A	QVQLVQSGGGVVQPGRSLRLSCKASGYTFTRYTMHWVRQAPGK					JA185
gh341E	QVQLVQSGGGVVQPGRSLRLSCKASGYTFTRYTMHWVRQAPGK					JA198
gh341*	QVQLVQSGGGVVQPGRSLRLSCKASGYTFTRYTMHWVRQAPGK					JA207
gh341*	QVQLVQSGGGVVQPGRSLRLSCKASGYTFTRYTMHWVRQAPGK					JA209
gh341D	QVQLVQSGGGVVQPGRSLRLSCKASGYTFTRYTMHWVRQAPGK					JA197
gh341*	QVQLVQSGGGVVQPGRSLRLSCKASGYTFTRYTMHWVRQAPGK					JA199
gh341C	QVQLVQSGGGVVQPGRSLRLSCKASGYTFTRYTMHWVRQAPGK					JA184
gh341*	QVQLVQSGGGVVQPGRSLRLSCSASGYTFTRYTMHWVRQAPGK					JA203
gh341*	QVQLVESGGGVVQPGRSLRLSCSASGYTFTRYTMHWVRQAPGK					JA205
gh341B	QVQLVESGGGVVQPGRSLRLSCSSSGYTFTRYTMHWVRQAPGK					JA183
gh341*	QVQLVQSGGGVVQPGRSLRLSCSASGYTFTRYTMHWVRQAPGK					JA204
gh341*	QVQLVESGGGVVQPGRSLRLSCSASGYTFTRYTMHWVRQAPGK					JA206
gh341*	QVQLVQSGGGVVQPGRSLRLSCSASGYTFTRYTMHWVRQAPGK					JA208
KDL	QVQLVESGGGVVQPGRSLRLSCSSSGFIFSSYAMYWVRQAPGK					

FIG. 5a

Application No.: 08/846,658

Title: Humanised Antibodies

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Docket No. CARP-0057

Atty: Doreen Yatko Trujillo

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	44	50	65	83	
Dkt3vh	GLEWIGYINPSRGYTNYNQFKDKATLT T DKSSSTAYMQLSSLT				
gH341	GLEWVAYINPSRGYTNYNQKFKDRFTISR D NSKNTLFLQMDSLR				JA178
gH341A	GLEWIGYINPSRGYTNYNQKVKDRFTIST D KSKST A FLQMDSLR				JA185
gH341E	GLEWIGYINPSRGYTNYNQKVKDRFTIST D KSKST A FLQMDSLR				JA198
gH341*	GLEWIGYINPSRGYTNYNQKVKDRFTIST D KSKNT A FLQMDSLR				JA207
gH341*	GLEWIGYINPSRGYTNYNQKVKDRFTISR D NSKNTLFLQMDSLR				JA209
gH341D	GLEWIGYINPSRGYTNYNQKVKDRFTIST D KSKNTLFLQMDSLR				JA197
gH341*	GLEWIGYINPSRGYTNYNQKVKDRFTISR D NSKNTLFLQMDSLR				JA199
gH341C	GLEWVAYINPSRGYTNYNQKFKDRFTISR D NSKNTLFLQMDSLR				JA184
gH341*	GLEWIGYINPSRGYTNYNQKVKDRFTIST D KSKST A FLQMDSLR				JA207
gH341*	GLEWIGYINPSRGYTNYNQKVKDRFTIST D KSKST A FLQMDSLR				JA205
gH341B	GLEWIGYINPSRGYTNYNQKVKDRFTIST D KSKST A FLQMDSLR				JA183
gH341*	GLEWIGYINPSRGYTNYNQKVKDRFTIST D KSKST A FLQMDSLR				JA204
gH341*	GLEWIGYINPSRGYTNYNQKVKDRFTIST D KSKST A FLQMDSLR				JA206
gH341*	GLEWIGYINPSRGYTNYNQKVKDRFTIST D KSKNT A FLQMDSLR				JA208
KDL	GLEWVAIIWDDGSDQHYADSVKGRFTISR D NSKNTLFLQMDSLR				

FIG. 5b

Application No.: 08/846,658

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	84	95	102	113		SEQ ID NO:
Dkt3vh	SEDS	AVYYCARYYDDHY	CL	DYWGQGTTLTVSS		
gH341	PEDTGVYFCARYYDDHY	CL	DYWGQGTTLTVSS		JA178	30
gH341A	PEDTAVYYCARYYDDHY	CL	DYWGQGTTLTVSS		JA185	12
gH341E	PEDTGVYFCARYYDDHY	CL	DYWGQGTTLTVSS		JA198	13
gH341*	PEDTGVYFCARYYDDHY	CL	DYWGQGTTLTVSS		JA207	14
gH341D	PEDTGVYFCARYYDDHY	CL	DYWGQGTTLTVSS		JA197	15
gH341*	PEDTGVYFCARYYDDHY	CL	DYWGQGTTLTVSS		JA209	16
gH341*	PEDTGVYFCARYYDDHY	CL	DYWGQGTTLTVSS		JA199	17
gH341C	PEDTGVYFCARYYDDHY	CL	DYWGQGTTLTVSS		JA184	18
gH341*	PEDTAVYYCARYYDDHY	CL	DYWGQGTTLTVSS		JA203	19
gH341*	PEDTAVYYCARYYDDHY	CL	DYWGQGTTLTVSS		JA205	20
gH341B	PEDTAVYYCARYYDDHY	CL	DYWGQGTTLTVSS		JA183	21
gH341*	PEDTGVYFCARYYDDHY	CL	DYWGQGTTLTVSS		JA204	22
gH341*	PEDTGVYFCARYYDDHY	CL	DYWGQGTTLTVSS		JA206	23
gH341*	PEDTGVYFCARYYDDHY	CL	DYWGQGTTLTVSS		JA208	24
KDL	PEDTGVYFCARDGGHGFCSSASCFGP	DYWGQGTTPVTVSS				10

FIG. 5c

DKT3 LIGHT CHAIN CDR GRAFTING

1. gL221 and derivatives

	1	24	34	42	
Dkt3vl	QIVLTQSPADMSASPG	EKVTMTCSASS.	SVSYM	NWYQQKSGT	
gL221	DIQMTQSPSSLSASV	GDRVTITCSASS.	SVSYM	NWYQQTPGK	
gL221A	<u>QIV</u> MTQSPSSLSASV	GDRVTITCSASS.	SVSYM	NWYQQTPGK	
gL221B	<u>QIV</u> MTQSPSSLSASV	GDRVTITCSASS.	SVSYM	NWYQQTPGK	
gL221C	<u>DIQ</u> MTQSPSSLSASV	GDRVTITCSASS.	SVSYM	NWYQQTPGK	
REI	DIQMTQSPSSLSASV	GDRVTITCQASQDI	IKYLN	NWYQQTPGK	

	43	50	56	85	
Dkt3vl	SPKRWIYDTSK	LAGVPAHFRGSGSGT	SYSLTISG	MEAEDAAT	
gL221	APKLLIYDTSK	LAGVPSRFSGSGSGT	DYFTISS	LQPEDIAT	
gL221A	APKRWIYDTSK	LAGVPSRFSGSGSGT	DYFTISS	LQPEDIAT	
gL221B	APKRWIYDTSK	LAGVPSRFSGSGSGT	DYFTISS	LQPEDIAT	
gL221C	APKRWIYDTSK	LAGVPSRFSGSGSGT	DYFTISS	LQPEDIAT	
REI	APKLLIYEASNLQ	AGVPSRFSGSGSGT	DYFTISS	LQPEDIAT (SEQ ID NO:8)	

	86	91	96	108	
Dkt3vl	YYCQQWSSNP	FTFGSGTKLE	INR		(SEQ ID NO:29)
gL221	YYCQQWSSNP	ETFGGQTKLQ	ITR		(SEQ ID NO:25)
gL221A	YYCQQWSSNP	ETFGGQTKLQ	ITR		(SEQ ID NO:26)
gL221B	YYCQQWSSNP	ETFGGQTKLQ	ITR		(SEQ ID NO:27)
gL221C	YYCQQWSSNP	ETFGGQTKLQ	ITR		(SEQ ID NO:28)
REI	YYCQQYQSLPY	TFGGQTKLQ	ITR		(SEQ ID NO:9)

CDR'S ARE UNDERLINED

FRAMEWORK RESIDUES INCLUDED IN THE GENE ARE DOUBLE UNDERLINED

FIG. 6

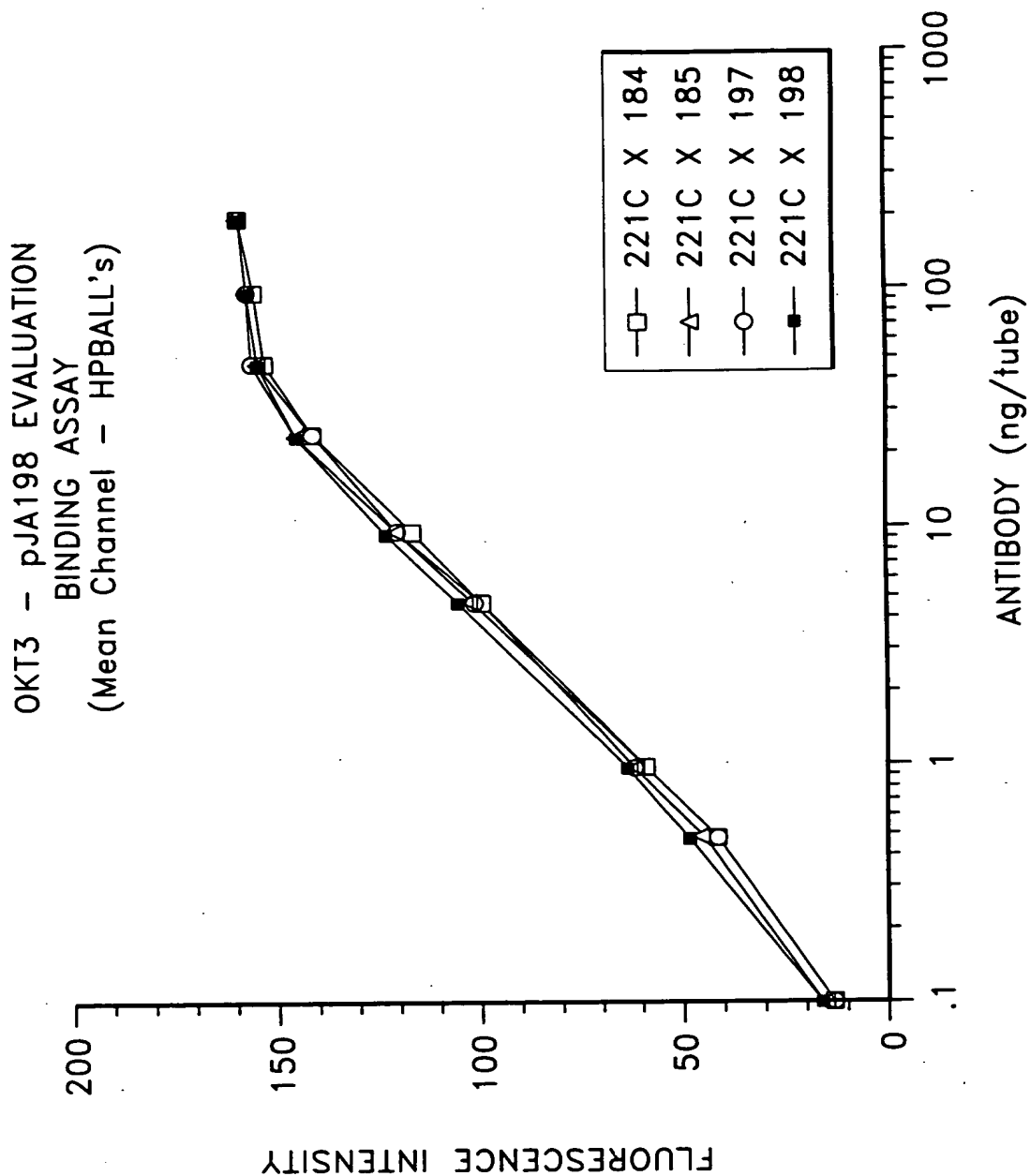


FIG. 7

OKT3 - pJA198 EVALUATION
 BLOCKING ASSAY
 (Mean Channel - HPBALL's)

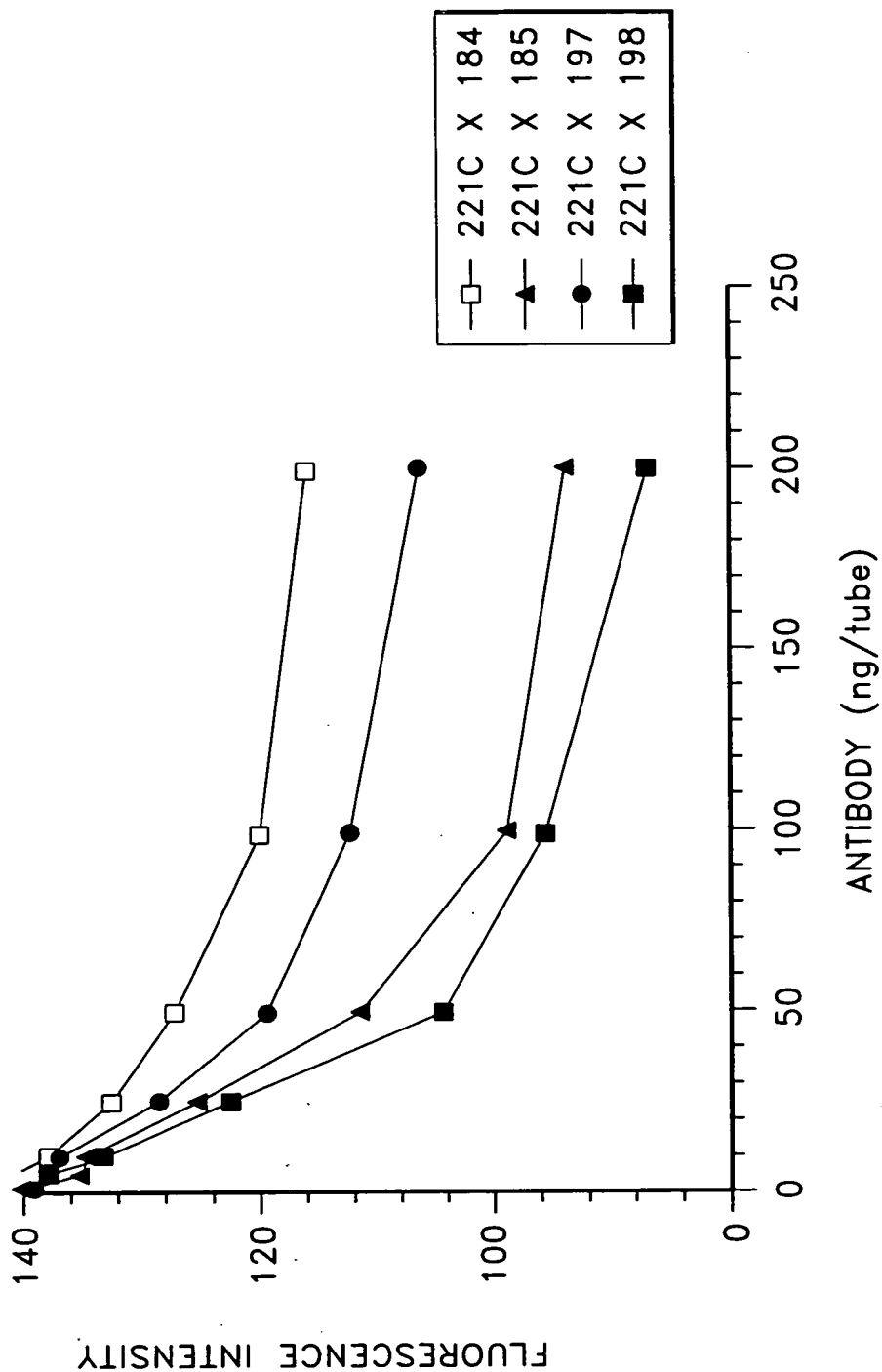


FIG. 8

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BLOCKING ASSAY
(Mean Channel - HPBALL's)

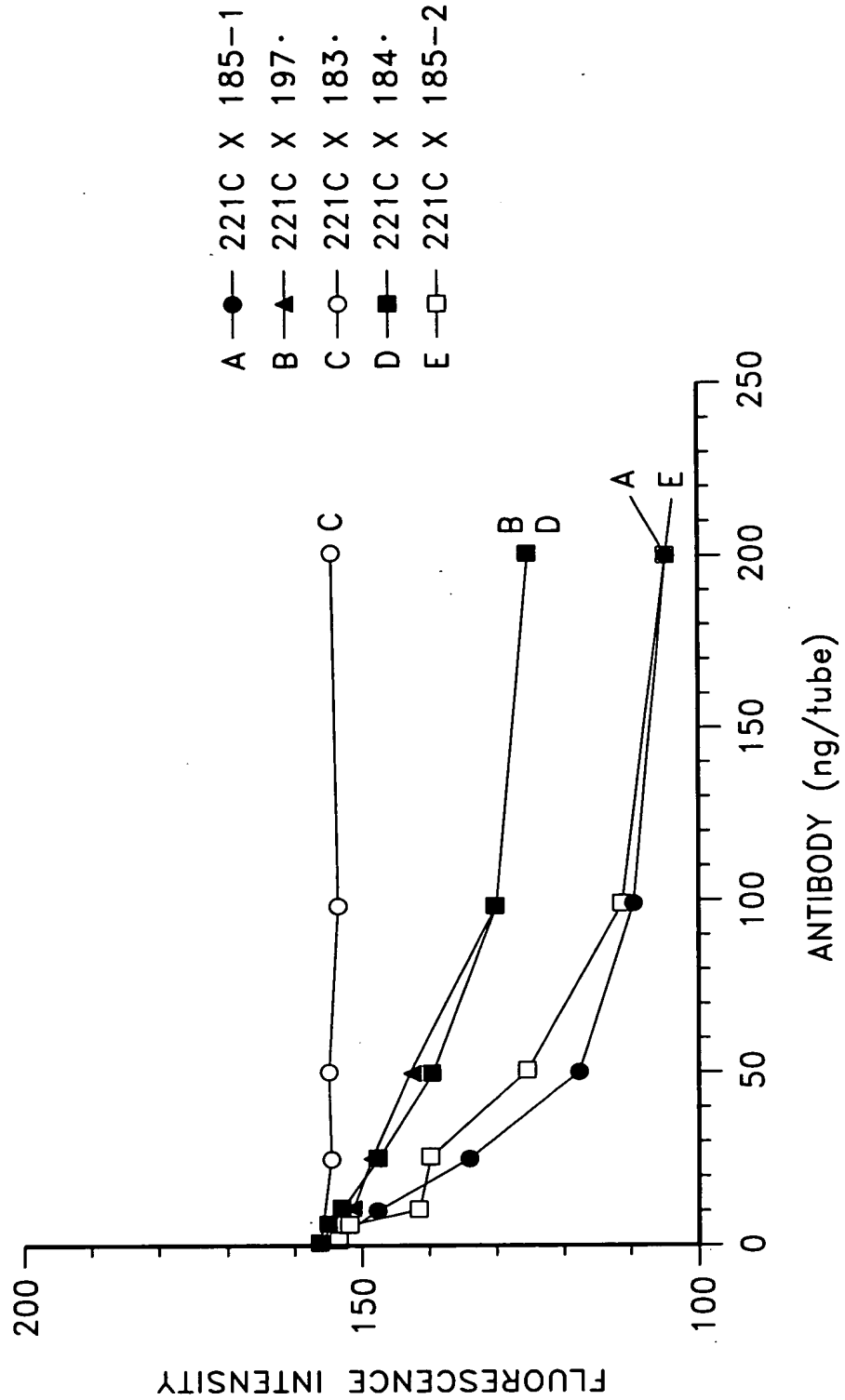
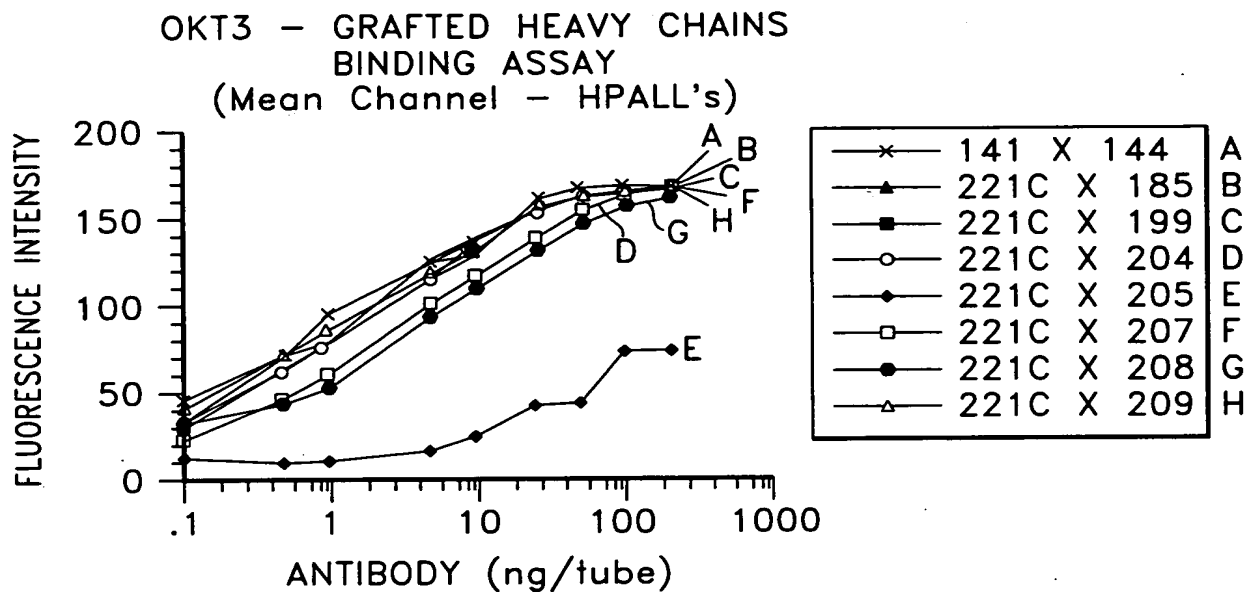


FIG. 9



—◆—	(205)	—, —, —, 24, 48, 49, 71, 73, 76, 78, 88, 91,
—●—	(208)	6, —, —, 24, 48, 49, 71, 73, —, 78, —, —,
—○—	(204)	6, —, —, 24, 48, 49, 71, 73, 76, 78, —, —,
—■—	(199)	6, 23, 24, 48, 49, —, —, —, —, —, —,
—□—	(207)	6, 23, 24, 48, 49, 71, 73, —, 78, —, —,
—▲—	(185)	6, 23, 24, 48, 49, 71, 73, 76, 78, 88, 91,
—△—	(209)	6, 23, 24, 48, 49, —, —, —, —, 78, —, —,
—x—	141 X 144	

FIG. 10a

Application No.: 08/846,658

Title: Humanised Antibodies

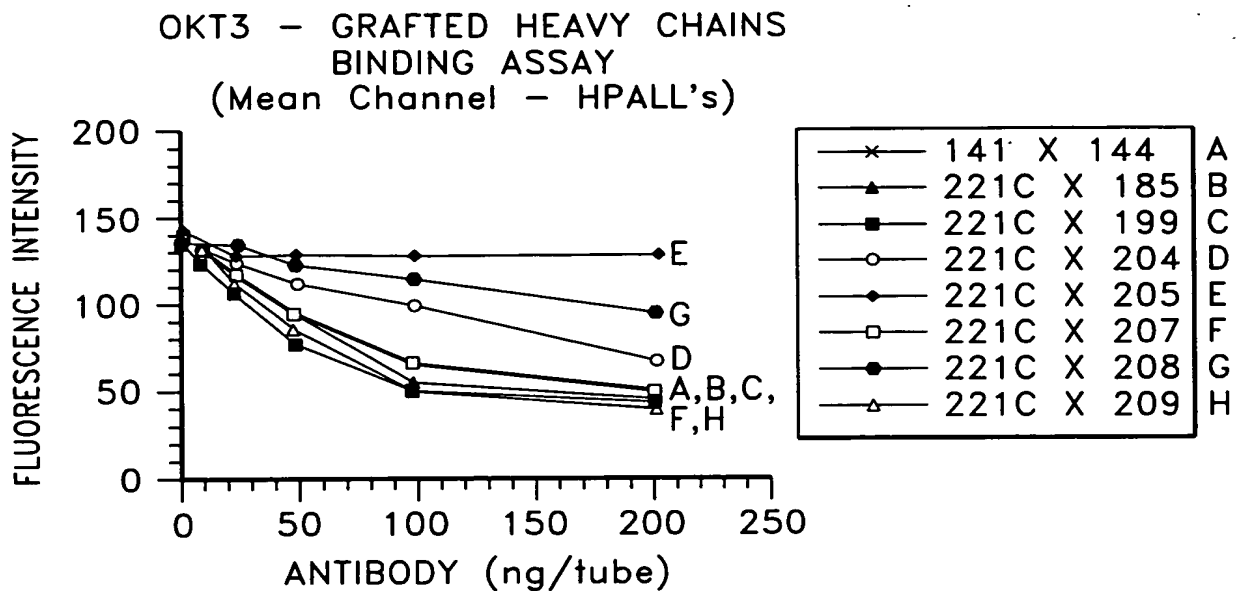
Inventors: John R. Adair, Diljeet S. Athwal and John S. Emtage

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—◆—	(205)	—, —, 24, 48, 49, 71, 73, 76, 78, 88, 91,
—●—	(208)	6, —, 24, 48, 49, 71, 73, —, 78, —, —,
—○—	(204)	6, —, 24, 48, 49, 71, 73, 76, 78, —, —,
—■—	(199)	6, 23, 24, 48, 49, —, —, —, —, —,
—□—	(207)	6, 23, 24, 48, 49, 71, 73, —, 78, —, —,
—▲—	(185)	6, 23, 24, 48, 49, 71, 73, 76, 78, 88, 91,
—△—	(209)	6, 23, 24, 48, 49, —, —, —, —, 78, —, —,
—x—	141 X 144	

FIG. 10b

OKT3 - GRAFTED HEAVY CHAINS
BINDING ASSAY
(Mean Channel - HPALL's)

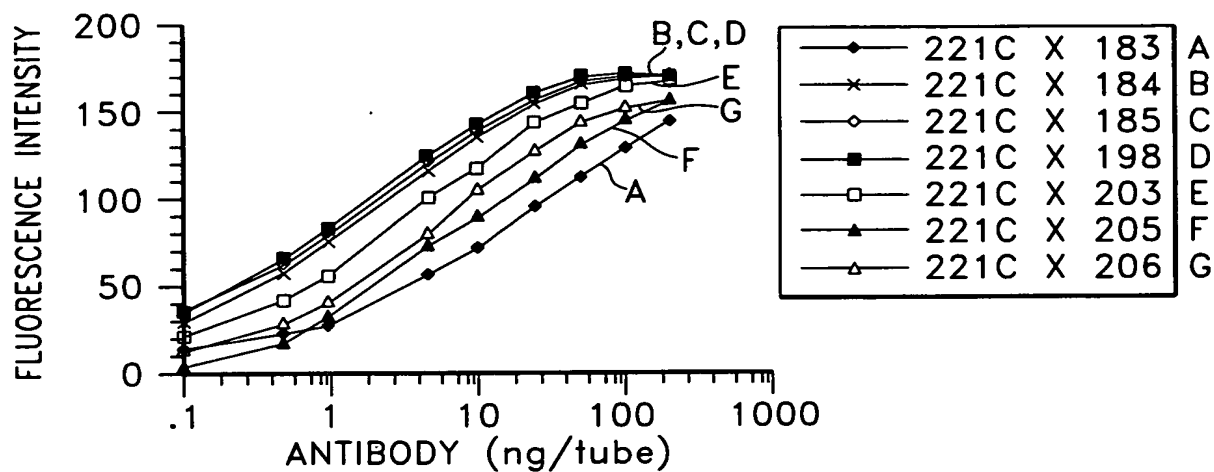
[illegible]

FIG. 11a

	(183)	--, --, ---, , 48, 49, 71, 73, 76, 78, 88, 91,
	(205)	--, --, 24, 48, 49, 71, 73, 76, 78, 88, 91,
	(184)	6, 23, 24, --, --, --, --, --, --, --, --, --,
	(206)	--, --, 24, 48, 49, 71, 73, 76, 78, --, --,
	(203)	6, --, 24, 48, 49, 71, 73, 76, 78, 88, 91,
	(185)	6, 23, 24, 48, 49, 71, 73, 76, 78, 88, 91,
	(198)	6, 23, 24, 48, 49, 71, 73, 76, 78, --, --,

FIG. 11b

Application No.: 08/846,658

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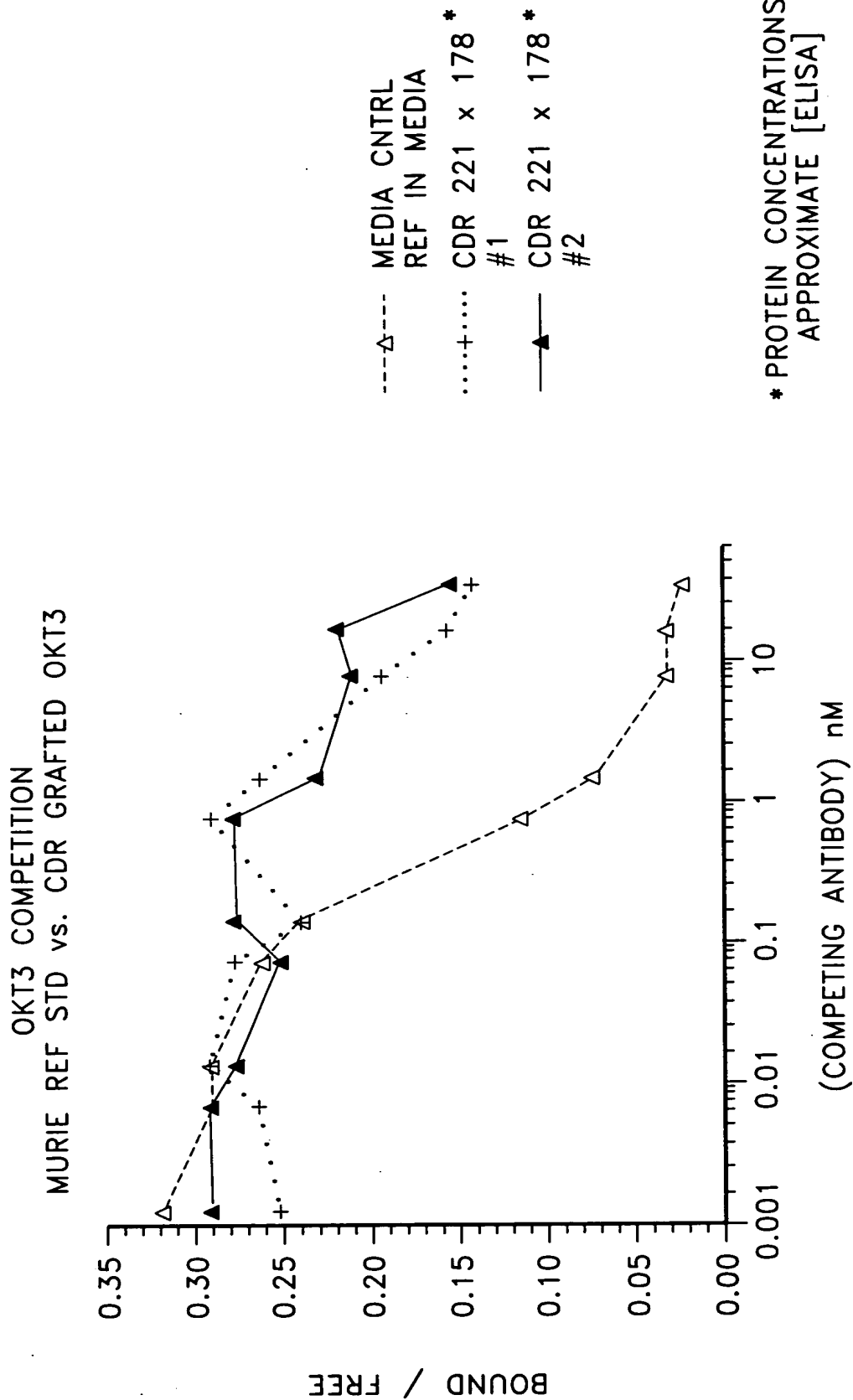


FIG. 12

Application No.: 08/846,658

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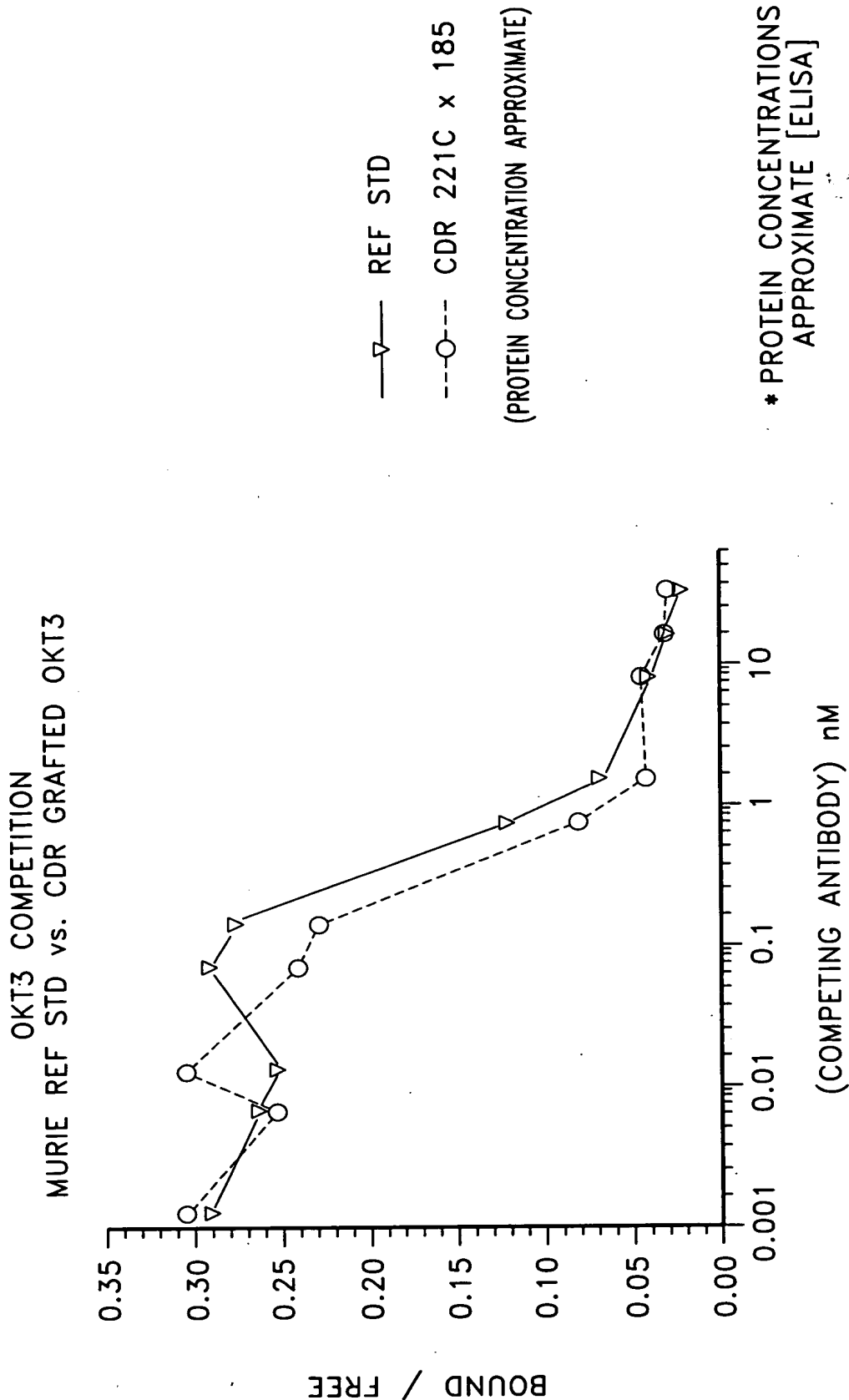


FIG. 13